

THE AMERICAN JOURNAL OF PHARMACY.

SEPTEMBER, 1888.

GRINDELIA ROBUSTA AND GRINDELIA SQUARROSA.

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From an inaugural essay.

Grindelia robusta being officinal, and no thorough investigation having been made, it was thought desirable to do so. An analysis was made in the chemical laboratory of the College, and under the direction of Professor Henry Trimble, to whom I am indebted for many valuable suggestions. An analysis of *Grindelia squarrosa* was also made at the same time, not only on account of its individual interest, but especially for purposes of comparison. The work, in general, was based on Dragendorff's Method of Plant Analysis.

DESCRIPTION OF THE DRUGS.

G. robusta and *G. squarrosa*, as found in the market, consist of the leaves and flowering tops of the herbs. They belong to the natural order Compositæ, and are found west of the Rocky Mountains, especially in California.

There being some uncertainty as to the means of distinguishing the two species, a few of the more important points of difference may be of interest.

The drugs from which each analysis was made were personally selected in the crude state from the large stock of a reliable house, and may be relied upon as genuine.

1. *G. robusta* is, as its name implies, a robust grower, with large numerous leaves; while *G. squarrosa* is more attenuated, the leaves smaller, and branches and leaves less numerous.

2. The color of *G. robusta*, as seen in the market, is of a greenish

brown; that of *G. squarrosa* is much lighter, the involucre and stems being of a straw color, the leaves pea-green.

3. The leaves of *G. robusta* are ovate, slightly serrate, sessile or clasping; those of *G. squarrosa* are lanceolate or obspatulate, more deeply serrate, and while the upper leaves may be sessile or clasping, those lower down are narrowed at the base to the midrib, which often extends half an inch or an inch from the stem before widening into the blade of the leaf.

4. The flower-heads of *G. robusta* are depressed globular, with the scales of the involucre closely appressed; those of *G. squarrosa* are nearly conical in shape, with the scales of the involucre extended or squarrose, giving the head somewhat the appearance of a burr.

PROPERTIES.

G. robusta has the reputation of being almost a specific for certain forms of asthma, and externally in rhus poisoning. *G. squarrosa* has similar properties, but is less known and used.

HISTORY OF PREVIOUS INVESTIGATIONS.

In 1876, Dr. C. J. Rademaker made a chemical analysis of *Grindelia robusta* (New Remedies, July, 1876). He exhausted the drug with a hydro-alcoholic menstruum, obtaining from the evaporated residue, by treatment with ether, "an oleo-resin having the physical appearance of balsam of tolu and the odor of resin of turpentine." The oleo-resin was treated for alkaloid by treating with acidulated water-filtering, rendering alkaline, and agitating with ether. An aqueous solution of the ethereal residue had "an alkaline reaction, and under the microscope showed well-formed prismatic crystals."

On treating for organic acids by acidulating the alkaline fluid from which the base and oleo-resin had been extracted, agitating with ether, and evaporating the ethereal layer, a residue was obtained, the aqueous solution of which had an "acid reaction, completely neutralized alkalies and formed salts. Under the microscope the acid showed well-formed acicular crystals."

Before my work was completed an analysis of *G. robusta* was made by G. Linwood Libby, an abstract of which is given in the Pharm. Era, January, 1888. He found an oleo-resin, an acid resin and a resin. He states that although he twice followed Dr. Rademaker's process carefully, he was unable to verify his results.

ANALYSIS.

For the quantitative analysis, 100 grams of each drug, in No. 80 powder, were used and subjected to the same treatment. The results were similar, hence the drugs will be considered together in the report. When not otherwise specified, the statements made apply to both. This is done to avoid repetition.

I. TREATMENT WITH PETROLEUM ETHER.

The drug was exhausted with petroleum ether (boiling point below 45°) in successive portions. The amount soluble in this menstruum is *G. robusta*—8.87 per cent. : *G. squarrosa*—5.94 per cent. This residue was found to consist of vegetable wax and fixed and volatile oils in the following proportions :

| | | | | | | | | |
|--------------------------|------|-------------|------------|------|-------------|-----------|------|----------|
| <i>G. robusta</i> , wax, | 0.41 | per cent. ; | fixed oil, | 8.27 | per cent. ; | vol. oil, | 0.19 | per cent |
| <i>G. squarrosa</i> , " | 0.36 | " | " | 5.42 | " | " | 0.16 | " |

The wax was of a white color, solid at ordinary temperatures, melted at about 53° C. ; did not saponify with an aqueous solution of soda, but did with an alcoholic solution of soda. The addition of barium chloride formed a barium soap, insoluble in ether. The alcoholic filtrate from the soap was treated with ether and the ethereal solution evaporated, leaving a solid, white residue, melting at about 50° C., pointing to cetyl as a base.

The fixed oil was solid at ordinary temperatures, melting at 37° C., and was of a brown color. It gave a brown color on the addition of sulphuric acid. The oil was treated with a solution of caustic soda, sp. gr. 1.26. No saponification occurred, even on boiling. On diluting largely with water, however, it saponified readily, giving off the strong odor of the drug. Salt was added in excess and the soap collected. The residue was filtered, evaporated and tested by the flame test with the borax bead for glycerin, but with negative results. The soap was decomposed with hydrochloric acid and distilled with water. The distillate had oil globules floating on its surface, demonstrating the presence of a volatile fat-acid. Its odor was aromatic and somewhat valerian-like. The yield from the amount examined was too small to determine its composition by ultimate analysis.

The non-volatile fat-acids were separated by fractional precipitation with acetate of magnesium and found to consist of a mixture of palmitic, stearic and oleic acids.

Small quantities of the volatile oils were obtained by distilling each drug with water and shaking the distillate with petroleum ether. The oils resemble each other closely. They have an agreeable aromatic, pungent, somewhat mint-like odor and burning taste.

II. TREATMENT WITH ETHER.

The petroleum ether remaining in the drug was evaporated, and the drug exhausted with successive portions of ether. Proportion extracted by this solvent:—

| | | |
|-----------------------|----------------------|-----------------------------------|
| G. robusta, | 4.02 per cent., | of which 3.80 per cent. is resin. |
| G. squarrosa, | 6.92 " " | 4.01 " " |

The resin is soft (about the consistency of styrax), of a greenish-black color, having a smooth bland taste to the tongue, but after a short time having a very irritating effect on the fauces. It has the odor of the drug. It melts at about 40° C. On the addition of sulphuric acid the resin dissolves with a brown color and a rise in temperature. Nitric acid (sp. gr. 1.42) cold, gives a yellow-green color; on warming, effervescence takes place, with evolution of brown fumes of NO₂ and a peculiar smell.

The resin dissolves completely in a weak solution of the caustic alkalies, indicating that it is an acid-resin. On neutralizing the resin with caustic alkali, concentrating and allowing to stand, prismatic crystals were obtained, colorless, with a cooling saline taste, and insoluble in hot and cold alcohol, chloroform and ether. A portion of the resin was treated with 20 per cent. alcohol, the residue treated with 50 per cent. alcohol, and so on with 75 per cent. and 94 per cent. 75 per cent. alcohol dissolved the larger portion, very little remaining; showing that a 75° menstruum would exhaust the drugs of their resinous constituents. The different fractions obtained have the same melting point and give the same color-reactions as the original resin.

A portion of the ethereal extract was concentrated and precipitated in distilled water, the resin collected, dissolved in a little alcohol and reprecipitated in water containing one per cent. sulphuric acid. Each of these aqueous solutions of the ethereal extract were treated with petroleum ether, benzol, chloroform and ether, successively, for alkaloids, glucosides, or bitter principles. The aqueous solutions were then rendered alkaline and again agitated with the same solvents, with negative results in each case, except that the chloroform residue

gave a slight reaction for a glucoside with Fehling's solution, being the same glucoside that was extracted more freely by alcohol and water.

III. TREATMENT WITH ALCOHOL.

The drugs, freed from ether, were exhausted with successive portions of absolute alcohol. Extracted from *G. robusta* 2.04 per cent. and *G. squarrosa* 2.67 per cent. The dried residue was of a resinous or extract-like appearance, of a brown color, and acrid taste. Its aqueous solution was colored greenish black by ferric chloride, foamed on agitation, had an acid reaction and was precipitated by acetate of lead. The acidified aqueous solution gave marked alkaloidal reactions with the following reagents: potassio-mercuric iodide, tri-iodide of potassium, phosphomolybdic acid, tannin, potassio-bismuthic iodide, and picric acid. From this evidence it was assumed that an alkaloid was present. The acidified aqueous solution was agitated successively with the solvents previously used; then the solution rendered alkaline and again treated with solvents. A slight residue was obtained with each solvent—largest with chloroform—of a yellow color, soft and sticky, and of a burning, very acrid taste, especially affecting the palate. An aqueous solution of these residues was of neutral reaction: on adding the smallest portion of acid it was rendered permanently acid, and with the reagents did not give as heavy alkaloidal reactions as did the liquid which had been agitated with the solvents. No different results were obtained on testing a solution of the residues in acidulated water. One pound of each drug was then exhausted with strong alcohol, the alcohol evaporated, and the syrupy extract poured into water acidulated with one per cent. of sulphuric acid. After standing for twelve hours, with frequent stirring, the liquor was decanted, filtered, and agitated with solvents as before, both in acid and alkaline condition. The results were the same as those of the previous trial. Five pounds of *G. robusta* were then exhausted with alcohol and given the same treatment, also adding to the list of solvents acetic ether, carbon disulphide and fusel oil. No alkaloid was obtained. A portion of the solution was neutralized, evaporated to dryness and the residue agitated with solvents, with still a negative result. Extraction from the drug by Prolius' fluid was tried, also without success. The methods used would undoubtedly have extracted an alkaloid had one been present, so it

is safe to say that none exists in these plants. The uniform positive reactions with the accepted alkaloidal reactions are difficult to explain, but they are probably caused by some albuminous matter peculiar to these plants.

The substance extracted by the various solvents was free from glucose until after boiling with dilute acid, showing that a glucoside had been extracted.

IV. TREATMENT WITH WATER.

| | G. robusta. | G. squarrosa. |
|--|-----------------|-----------------|
| Total extract..... | 12.16 per cent. | 12.88 per cent. |
| Containing ash..... | 2.80 " | 2.51 " |
| a. Mucilage and carbohydrates precipitated | | |
| by alcohol..... | 2.17 " | 1.93 " |
| Yielding ash..... | 0.5 " | 0.67 " |
| b. Glucose..... | 1.26 " | 1.90 " |

Saccharose was not present.

(c) *Saponin*.—From the foamy, soapy-like character of the aqueous extract on agitation, as well as the taste of the resin and of the glucoside extracted, it was inferred that saponin or an allied body was present. A quantitative estimation by the method adopted by Christophsohn and Otten,¹ was made with the following results: *G. robusta*, 2 per cent.; *G. squarrosa*, 0.82 per cent. saponin.

As far as I have been able to learn, these are the first plants of the natural order composite in which a saponin-like body has been found, and is therefore unique. It does not give the color-reaction of true saponin with sulphuric acid, but it possesses its attributes to a marked degree. It has its soapy character; acrid taste, affecting the fauces; is precipitated by baryta water; forms crystals with alkaline hydrates, and has a slight acid reaction. It is undoubtedly this that gives the acid reaction to the aqueous solutions of the various extracts. It was thought at first that this was due to the presence of organic acids; but on adding barium carbonate to the solution, it was not neutralized, even on boiling. Calcium carbonate also had no effect. Colorless, needle-shaped crystals of this saponin-like body were obtained by agitation with acetic ether (which had been freshly distilled over lime) evaporating, treating the residue with chloroform and evaporating in a dessicator over sulphuric acid. The principle in the two plants appears to be identical, and the name of

¹ Dragendorff's Plant Analysis, page 68.

grindelin is suggested for it. It is probable that the medical properties of the plants are due to this substance.

To a portion of the aqueous solution, sulphuric acid was added, and allowed to stand in a cool place for 48 hours. At the end of that time the liquid was observed to have a large number of minute acicular crystals floating in it. These were filtered off and dried, and on opening the filter, they separated in a thin, papery cone, glistening like benzoic acid. These crystals were thought to be the decomposition-product of *grindelin*, brought about by the action of the dilute acid in the cold, glucose being liberated.

To determine whether or not such was the case, a gravimetric estimation of the glucose in the liquid producing the crystals, and in the aqueous solution to which no acid had been added, was made. The supposition was verified, as the former yielded 0.26 per cent. more glucose than the latter. On boiling a solution with dilute acids, a white insoluble substance separates out, which on standing unites into a resin, having properties identical with that found in the drug. The theory is advanced that the resin found in the drug is wholly a decomposition product of *grindelin*, the greater part of the glucose set free being used by the plant as a necessary constituent to its growth and development.

(d) *Tannin*. A quantitative estimation of tannin was made with gelatin, in the presence of alum. An immediate precipitation took place in the solution of *G. robusta*. After 12 hours this was filtered off, washed, dried and weighed. 50 per cent. of the dried residue was calculated as tannin, giving a yield of about $1\frac{1}{2}$ per cent.

No tannin was found in *G. squarrosa*, no precipitate having formed at the end of 12 hours.

V. TREATMENT WITH DILUTE CAUSTIC SODA.

The drugs were exhausted with a dilute solution of caustic soda, and the substances soluble therein estimated as pectin, albuminoids, and allied bodies. *G. robusta* yielded 5.68 per cent; *G. squarrosa* 3.56 per cent.

VI. TREATMENT WITH DILUTE HYDROCHLORIC ACID.

No starch is present in either drug.

Total extracted by above solvent: *G. robusta* 2.17 per cent., of which 1.06 per cent. is calcium oxalate. *G. squarrosa* 4.94 per cent., of which 1.00 is calcium oxalate.

VII. DETERMINATION OF LIGNIN AND CELLULOSE.

The lignin was estimated by maceration with chlorine water. *G. robusta* 3.40 per cent., *G. squarrosa* 5.71 per cent.

The residue was macerated with nitric acid and potassium chlorate.

G. robusta, intercellular substance, &c., 30.24%; sand, cellulose, &c., 12.53%.
G. squarrosa, " " " 25.44 " " " 15.02

VIII. ESTIMATION OF MOISTURE AND ASH.

G. robusta, moisture 11.12 per cent., ash 7.77 per cent.
G. squarrosa, " 11.7 " " " 5.22 " "

A qualitative analysis of the ash showed the presence of potassium, sodium, calcium, magnesium and iron as bases, and sulphuric, hydrochloric, carbonic and phosphoric acids.

Not having been able to verify Dr. Rademaker's results, I exhausted 1 lb. of *Grindelia robusta* with 75 per cent. alcohol and made a careful analysis according to his process, the results corresponding with my previous work. The substance which was extracted for "alkaloid" when treated with distilled water gave a neutral reaction; on adding one drop of water acidulated with sulphuric acid (1:500) the solution was rendered permanently acid. It was then tested, before and after boiling, with dilute acid and found to be a glucoside. The substance which came out as "organic acid," was of acid reaction, did not neutralize barium carbonate, and also reduced Fehling's solution after boiling with dilute acid, corresponding to the properties of the saponin-like body before referred to, and evidently identical with it.

NOTE BY THE EDITOR.—*The Pharmaceutical Era*, June, contains an analysis of *Grindelia robusta* by John L. Fischer, the results of which, compared with those of Mr. Clark, are as follows:

| | Clark. | Fischer. |
|--------------------------------|--------|----------|
| Petroleum extract..... | 8.87 | 8.50 |
| Ether extract..... | 4.02 | 10.05 |
| Alcohol extract | 2.04 | 6.00 |
| Water extract..... | 12.16 | 13.05 |
| Dilute soda solution | 5.68 | — |
| Dilute acid solution..... | 2.17 | 2.02 |
| Lignin | 3.40 | 47.00 |
| Intercellular substances | 30.24 | |
| Cellulose | 12.53 | |
| Moisture | 11.12 | 11.08 |
| Ash..... | 7.77 | — |

By dissolving the water extract in distilled water, rendering the solution alkaline, and agitating with ether, Fischer obtained a principle, *grindeline*, which had an alkaline reaction and neutralized acids, the sulphate crystallizing in groups of acicular prisms; it is described as being bitter, soluble in ether, alcohol and water, and precipitated by tannin, potassio-mercuric iodide, picric acid, potassium bichromate, iodine, and the chlorides of gold and platinum. Alkalinity excepted, these properties agree with those of the yellow sticky mass obtained by Mr. Clark from the alcohol-extract by a process similar to the foregoing.

NOTES ON THE ESSENTIAL OILS OF BAY, PIMENTA AND CLOVES.

BY GEO. M. BERINGER, A. M., Ph. G.

The U. S. Pharmacopœia describes oil of myrcia as "a brownish or dark brown liquid of an aromatic, somewhat clove-like odor, a pungent, spicy taste, and a slightly acid reaction. Sp. gr. about 1.040, soluble in an equal weight of alcohol. With an equal volume of a concentrated solution of potassa it forms a semi-solid mass."

This description is incorrect in at least one important point, namely, the specific gravity stated, and misleading, if not absolutely erroneous in its statement regarding the solubility. These errors have been copied into the dispensaries and various text books without comment or correction.

The usual adulterants for this oil are the oils of cloves, pimenta and copaiba. The detection of these by color reactions or other chemical tests is difficult. The odor, specific gravity and solubility are the most important characteristics for recognizing adulteration, and so it is of the greatest importance, that our Pharmacopœia should be correct in these statements.

In the AMERICAN JOURNAL OF PHARMACY, (1887, page 286), the writer called attention to the fact that two samples of oil of bay examined, showed a sp. gr. of 0.975 and 0.9945. Recently Messrs. Dodge & Olcott have called attention to this error (*Drug. Circ.*, July, 1888), stating as the result of their extended experience in distilling this oil, that the correct sp. gr. is near 0.965 at 60° F.

The authority for the pharmacopœial statement the writer has been unable to discover. Prof. Markoe (*Proc. Amer. Phar. Assoc.*, 1877)

Oil of pimenta makes a clear solution in absolute alcohol and in 95 or 85 per cent. alcohol in all proportions. It makes a clear solution with three volumes of 60 per cent. alcohol, which is not rendered cloudy on further addition of the alcohol. With five volumes of 50 per cent alcohol it makes a turbid, milky solution without separation of oil globules, the opalescence diminishing on increasing the alcohol, a clear solution being produced when thirty volumes of diluted alcohol have been added.

Oil of cloves is soluble in all proportions of absolute alcohol and 95 per cent. alcohol. Soluble in equal volume of 85 per cent. alcohol, which is not rendered milky on further addition. Soluble in three volumes of 60 per cent. alcohol, the solution being rendered milky on further addition of alcohol.

A mixture of 80 per cent. oil of bay and 20 per cent. oil of pimenta is soluble with slight milkiness in equal volume of alcohol. A mixture of 50 per cent. of each gave but very slight milkiness, practically a clear solution, in equal volume of alcohol, but on adding more alcohol the milkiness becomes quite apparent. Mixtures of oil of bay with oil of cloves act similarly.

Oil of bay yields a clear solution in ether, but on diluting with 85 per cent. alcohol the solution is rendered cloudy, and on standing it gradually becomes clear, depositing a white film. Oil of bay yields a clear solution in benzin, chloroform and amylic alcohol; a milky solution in absolute alcohol, alcohol, methylic alcohol, turpentine, benzol, carbon bisulphide, glacial acetic acid, acetic ether and acetone.

Oil of pimenta yields a clear solution in ether, which remains clear on the addition of (85 per cent.) alcohol. It also yields a clear solution in benzin, benzol, chloroform, amylic alcohol, methylic alcohol, glacial acetic acid, acetic ether and acetone. Slightly milky in carbon bisulphide. A clear solution in equal volume of turpentine, but rendered milky on further addition.

Oil of cloves yields a clear solution in ether, not rendered milky on adding 85 per cent. alcohol. It yields a clear solution in chloroform, amylic alcohol, methylic alcohol, glacial acetic acid, acetic ether and acetone. Slightly milky with benzin; slightly milky with benzol, and not becoming clear by adding five times the volume of benzol; a milky solution in carbon bisulphide and turpentine.

I have found the following test of value in detecting the adultera-

The U. S. P. describes oil of cloves, as well as the oils of bay and pimenta, as slightly acid. The German Pharmacopœia states, "oil of cloves does not redden litmus." The following delicate reaction served to show the distinct acidity of these three oils. Ten drops of the oil was thoroughly shaken with half a fluidounce of boiling, distilled water, and when cold, filtered through a moistened filter. To one drachm of this filtrate was added, drop by drop, a small quantity of a very weak solution of phenolphthalein, made by adding 4 drops of one per cent. solution of phenolphthalein to a half fluidounce of water, and reddening by adding a couple of drops of liquor potassæ. Each fluid drachm of the aqueous solution of the oil was found sufficient to decolorize from 3 to 6 drops of this reagent, the color being again produced on adding a drop or two of very dilute solution of potassium hydrate.

BISMUTH SUBNITRATE.

BY FRANK X. MOERK, PH. G.

In calculating a formula conforming to suggestions made in the last number of this journal it was found that the figures relating to the U. S. P. (1870) formula, represented parts in one and not parts in one hundred, hence, the conclusions based on these figures are erroneous.

The conditions necessary to produce a compound of the formula BiONO_3 were ascertained by making a number of preparations, preceded, however, by some experiments showing the effect of NH_4NO_3 in neutral, acid and alkaline solutions upon a subnitrate of bismuth containing 11.71 per cent. oxide. The strength of the NH_4NO_3 solutions varied from 10 per cent. to 0.2 per cent.

In neutral solutions, there was no abstraction of acid noticeable, by reaction with litmus or by addition of NH_4OH to filtrate, in the cold; on warming all of the solutions reacted with litmus and NH_4OH , the more dilute the solution, the stronger the reaction. Dilute nitric acid, even in very minute quantities gave acid reaction and filtrate on addition of NH_4OH became cloudy, indicating that oxide or hydrate did exist with an acid nitrate, and, that the base and the acid salt did not react on each other.

Dilute ammonia water produced with the stronger ammonium nitrate solutions, an alkaline reaction not disappearing, even after standing several hours.

The specimens were made by varying the acidity of the mixed bismuth nitrate and ammonia solutions: No. 1, was of neutral reaction; No. 2, faintly acid; No. 3, the preceding while still moist treated with a slight though decided excess of nitric acid; No. 4, made by pouring the bismuth nitrate solution into the diluted ammonia and acidulating with HNO_3 ; No. 5, contained about $\frac{1}{2}$ per cent. free HNO_3 ; No. 6, contained 1 per cent. free HNO_3 . The mixtures were poured into small percolators and, after draining, washed with 0.2 per cent. NH_4NO_3 solution. In the first four samples little more than the quantity equal to the retained solution had to be added before the washings gave an entirely neutral reaction; in the last two, after adding more than twice this quantity the washings were decidedly acid and the ammonium nitrate was present in no larger quantity than corresponded to the solution used in washing, showing the 0.2 per cent. solution of NH_4NO_3 removed part of the acid from the precipitates. The washing was stopped and after draining the precipitate, this was dried as much as possible by pressing between filter paper, finally at a temperature below 70°C .

The amount of ammonium nitrate remaining in the dry product was inconsiderable.

In appearance Nos. 4 and 6 were the handsomest products, being almost a pure white; the others had a more or less yellowish tint dependent on amount of oxide contained in them. No. 6 on heating to drive off the moisture did not deepen in color, while No. 4 did, thus betraying the amount of oxide it contained.

| | Bi_2O_3 | N_2O_5 | H_2O | Bi ONO_3 | Bi_2O_3 |
|------------|-------------------------|------------------------|----------------------|-------------------|-------------------------|
| No. 1..... | 87.60 | 9.94 | 2.47 | 53.01 | 44.53 |
| " 2..... | 86.55 | 10.91 | 2.50 | 58.19 | 39.27 |
| " 3..... | 80.35 | 16.35 | 3.13 | 87.20 | 9.50 |
| " 4..... | 80.20 | 16.18 | 3.43 | 86.29 | 10.09 |
| " 5..... | 79.40 | 17.28 | 3.25 | 92.16 | 4.52 |
| " 6..... | 79.15 | 18.10 | 2.50 | 96.53 | 0.72 |

These results show that even in the presence of several per cent. of ammonium nitrate ammonium hydrate readily unites with the acid of the freshly precipitated salt, giving a very basic product; that Bi ONO_3 can only be obtained from decidedly acid solutions; that the product must be very sparingly washed (best by displacement in a percolator); that dilute NH_4NO_3 solution containing less than 0.5 per cent. will remove acid from Bi ONO_3 (result of experiments with

No. 6); and, lastly, that the U. S. P. (1870) formula, containing a little over one per cent. free HNO_3 will give a good product, losing, however, a portion of the water whilst drying.

The commercial products analyzed, resembling in composition Nos. 3 and 4 of the above, are very likely made by using the commercial water of ammonia, which is stronger than the officinal—10 per cent. of NH_3 .

The U. S. P. (1870) product is being examined in the laboratory by a senior student and for this reason no specimen made strictly according to those directions was examined by me.

PREPARATION OF C. P. HYDROGEN PEROXIDE FROM THE COMMERCIAL ARTICLE.

BY DR. MANN.

Translated from *Chemiker Zeitung*, 1888, p. 857.

The increased use of this preparation as an antiseptic in wound treatments has caused the study of making a pure product. The commercial article may contain HCl , H_2SO_4 , H_3PO_4 , HF , Al_2O_3 , MgO , K_2O and Na_2O as prepared for various purposes; generally CaO , derived from the water, and, if carelessly prepared, BaO and traces of Fe , Cu , Pb , Mn , etc. The following process will remove all of these, if present.

To the commercial preparation, containing about 3 per cent. H_2O_2 $\frac{1}{4}$ per cent. of pure concentrated H_3PO_4 is added after which the solution is rendered *exactly neutral* by addition of $\text{Ba}(\text{OH})_2$. This is the important step of the process having for its object the precipitation of the phosphates of the heavy as well as of the alkaline-earth metals. The time required for the neutralization should be at least 15 minutes during which period the liquid should be stirred continuously; a turbidity will occur and on 3–5 minutes standing the precipitate will deposit, from which the supernatant clear liquid is decanted or separated by filtration. The filtrate is poured, with continual agitation, into a cold saturated solution of $\text{Ba}(\text{OH})_2$, a precipitate of hydrated BaO_2 , in pearly laminae readily separates; H_2O_2 (the filtrate) is added as long as a precipitate forms, this, toward the end of the process, only takes place on thorough stirring of the liquid; excess of H_2O_2 should be avoided. The precipitate is washed with distilled water by decantation until only Ba can be detected in the washings.

100 parts of distilled water are mixed with 10-12 parts of pure concentrated H_2SO_4 and to this is added, drop by drop, the BaO_2 mixed with sufficient distilled water to form a thin paste until the acid is almost neutralized. The BaO_2 if added in too large portions acts decomposingly on the H_2O_2 formed. The last traces of H_2SO_4 are best neutralized by cautious addition of $\text{Ba}(\text{OH})_2$; after standing 24 hours the clear liquid is tested for Ba and H_2SO_4 and, if free from both, the liquid is syphoned off and, if necessary, filtered. Should either be present it would have to be removed by addition of the proper reagent, and the precipitate separated.

The H_2O_2 , thus purified, contains about 3 per cent. and will stand the most rigorous tests for purity and stability.

ABSTRACTS FROM THE FRENCH JOURNALS.

Translated for the AMERICAN JOURNAL OF PHARMACY.

EMULSIFYING MIXTURE.—The following is recommended by Nicot for making emulsions and for neutralizing the taste of oily and resinous drugs: Bark of quillaia saponaria, 20 gm.; balsam of tolu, 200 gm.; vanilla, 5 gm.; peel of two lemons; alcohol of 80%, 1 litre. The bark is bruised with the balsam and vanilla; the peel is added in small pieces, and the whole is then macerated with alcohol for 10 days; filter. This tincture will quickly emulsionize ol. ricini, copaiba, scammony, etc. For ol. ricini, 30 gm., use 2 gm. of the emulsive mixture; mix rapidly in a mortar and add by degrees a syrup composed of syr. simp., 40 gm.; aq. aurant. flor., 10 gm.¹—*Bull. gén. de therap.*, July 30, 1888.

PREPARATION OF FRUIT SYRUPS.—The pure juice contains carbonic acid; the sugar is usually added while the juice is cold, and when heat is added, the gas, being unable to escape from the thick liquid, tends to raise a portion of the mass from the bottom of the vessel. The mixture thus becomes overheated and causes the formation of caramel. M. Manch (*J. de Ph. et de Ch.*, July 15) recommends that the carbonic acid be driven off the juice, by heat, before the sugar is added, and the loss made up with distilled water.

¹See also paper by H. Collier in *AMER. JOUR. PHARM.*, 1880, pp. 41-44.

X UNALTERABLE SOLUTION OF PROTIODIDE OF IRON.—The formula recommended by Nicot is : Sugar, 4 gm. ; iodine, 5 gm. ; iron reduced by hydrogen, 8 gm. ; distilled water, 40 gm. ; pure glycerin, 110 gm. Mix the iodine and sugar in a porcelain mortar, adding the iron by degrees. Heat gently in a capsule stirring with a glass rod, and filter to separate the excess of iron ; then add the glycerin. The mixture should weigh 150 gm. The syrup is made by adding 6 gm. of this to 100 of syrup.¹—*Bull. gén. de thérap.*, July 30, 1888.

ACTION OF COLD UPON FERRIC SOLUTIONS.—M. Languepin submitted to cold a 30 to 100 solution of sulphate of protoxide of iron which had been exposed to the light while badly corked, and was much oxidized. The liquid consolidated in a greenish-white mass ; upon thawing it had the greenish color of protosulphate of iron. The ochre-colored deposit on the inside of the bottle had disappeared. A similar solution containing 1 to 100 of tartaric acid had also turned yellow, but became green under the influence of cold. It is curious that after undergoing this desoxidation the solutions remained unaltered for a long time. The writer observed that in using them (for photographic purposes) their strength was slightly impaired.—*Bull. de la Soc. de Ph., Bordeaux*, June, 1888.

X SULPHURIC ACID MADE BY A NEW METHOD.—Carl Polony of Vienna gives the process as follows : Sulphate of lime in small pieces is placed in a crucible and exposed for 3 hours to a temperature varying between 600° and 1500° C., and at the same time to a jet of superheated steam, when the sulphate decomposes, forming sulphuric acid and hydrated lime. The acid vapors are concentrated by the usual methods. According to the *Monit. des prod. chim.*, the sulphates of sodium, barium and strontium may be used in the same way.—*Nouv. Rem.*, Aug. 8, 1888.

CAY-CAY OR THE FAT TREE OF INDO-CHINA is described in the *Bull. de la S. des études indo-chinois* as being plentiful in Cochin China, Cambodia and Annam, where it attains a height of 40 metres and a diameter of 1 m. 20. Its fruit contains an oily almond which

¹ This is considerably weaker than the *sirop d'iodure de fer* of the French Codex, 1000 gm. of which must contain 4.10 gm. iodine. For the same weight of finished syrup the U. S. P. requires 82.0 gm. iodine.—Editor AMER. JOUR. PHAR.

the monkey and wild boar eat with avidity. Brousmiche and Lanesan class it under the rutaceæ as *Irvingia harmandiana*. The natives gather, bruise and heat the fruit and express the oil, which hardens into a waxy mass. The Annamites get but 20 per cent. of fat from it. By treating with sulphide of carbon, however, 52 per cent. of fat may be extracted. The fat is not a true wax, but resembles butter of cacao, for which it may become a substitute. It melts at 38° and solidifies at 35°, and in dry distillation gives acrolein.¹—*Rev. Scientifique; Nouv. Rem.*, June 24, 1888.

GALACTOSE AND ARABINOSE.—At a meeting of the Paris Society of Pharmacy, July 4th, M. Bourquelot said that chemists are not agreed concerning the susceptibility of galactose to fermentation. He explains the disagreement as follows: Galactose does not ferment when it is pure; it will undergo alcoholic fermentation, however, whenever it contains traces of glucose. Levulose and maltose present the same phenomenon. Writers also contest the bi-rotary power of arabinose; they are in error. The reason they have not observed it is because the conditions were defective. It is indispensable to take the rotary power immediately after preparing the solution; the power attains its inferior limit within half an hour. M. Bourquelot added that with maltose, glucose and galactose,—which all possess a double rotary power—heat acts in a different manner. In maltose the power is weakest at the time of manufacture, galactose and glucose act like arabinose.—*Arch. de phar.*, Aug. 5, 1888.

GRANDIFLORINE.—M. D. Freire (*Compt. Rend., Acad. des Sci.*) gives this name to a substance he has obtained from the fruit of *Solanum grandiflorum*, var. *pulverulentum*. He treated the sarcocarp with water and hydrated lime and evaporated to dryness. This gave a residuum which was exhausted with absolute alcohol; evaporation of the filtered liquid separates a resinous matter; after cooling, the nearly solid residuum is treated by dilute hydrochloric acid, which dissolves the alkaloid but leaves the resinous matter. The solution is decolorized and precipitated by ammonia. The alkaloid, dried over sulphuric acid, is white, bitter, insoluble in water, and soluble in alkalies and dilute acids. Heated with hydrated potash, it sets free ammonia, and the solution gives alkaloidal reactions. With sulphuric acid it gives

¹ For an account of cay-cay wax by J. B. Vignoli see AMER. JOUR. PHAR., 1886, p. 409.

a yellow color, deepening into red. With sulphuric acid and binoxide of manganese the yellow color changes to green and then to violet. Concentrated nitric acid gives reddish purple. The author says the substance is a powerful intoxicant and the fruit kills animals which eat of it.—*Nouv. Rem.*, June 24, 1888.

ACTION OF SULPHATE OF SPARTEINE.—Dr. Pawinsky, in an elaborate study of this drug (*Gaz. Lekars*, 1888), arrives at the following conclusions, based (clinically) upon experiments in 33 cases. In small doses of 2 or 3 cgm. or 6 to 8 cgm. daily it slows and strengthens the cardiac contractions. Doses of 8 to 12 cgm. or 1 gm. daily paralyze the heart-action; the pulse becomes slow, weak and arhythmic. Small doses irritate the pneumo-gastric, large ones paralyze it. Small doses augment the tonicity of the vessels; the effect is observed in 40 minutes after ingestion. No cumulative action was observed, or gastric disturbance. The author cannot say that sparteine has a direct diuretic action, but it favors diuresis and dissipates œdema and sanguineous stasis.—*Bull. gén. de thérap.*, July 15, 1888; see also AMER. JOUR. PHAR., 1886, p. 103, and 1887, p. 157.

GLEANINGS FROM THE GERMAN JOURNALS.

BY FRANK X. MOERK, PH. G.

Tincture of guaiac, a sensitive reagent for pus. The urine is filtered and a little of the reagent poured over the moist filter, a beautiful blue color is produced in presence of pus. Moderate warming favors whilst excessive heat entirely prevents the reaction. Reducing agents and caustic alkalies also prevent it. Saliva, nasal mucus, and milk also give the reaction although not so intense.—*Vitali (Bollet. Farm.) Rundsch.*, 1888, p. 531.

Olea Ætherea sine terpeno is the name proposed by Dr. Schweisinger for concentrated volatile oils made so by the removal of the non-fragrant hydrocarbon, and which represent from two to thirty volumes of the ordinary essential oils. Thus one volume of the concentrated oil represents two volumes of the oils of anise, cassia, fennel, ginger-grass, mentha crispa, mentha piperita, cloves, sassafras and star anise; two and one-half volumes of the oils bergamot, caraway and lavender; four volumes of cumin and rosemary; five volumes of thyme; six volumes of coriander; eight volumes of calamus; ten

volumes of absinth; twenty volumes of juniper; thirty volumes of angelica, lemon and orange.

They are more permanent, possess greater solubility in alcohol and water, have a finer odor rendered prominent only on great dilution, and are of constant composition, thus enabling the specific gravity and boiling point to be used as tests of purity. The use in pharmacy suggested is for medicated waters made by agitation of the oils with distilled water and filtering; also for elæosacchara, etc. They should be kept in the dark.—*Pharm. Centralk.*, 1888, No. 25.

An adhesive mixture consisting of rock candy 30 parts, dissolved in solution silicate of sodium 100 parts, is recommended by Kayser in *Bayer. Gew. Ztg.*, for the adhesion of paper on paper, leather, metal (tin boxes) and wood.—*Rundsch.*, 1888, p. 574.

Nylander's Sugar Test. 2 gm. bismuth subnitrate, 4 gm. rochelle salt, 100 gm. solution of soda (8 per cent.) Advantages: Easy preparation, stability and delicacy (0.025 per cent. can still be detected). (See *AMER. JOUR. PHAR.*, 1887, p. 396.)—*Pharm. Post*, 1888, p. 427.

Tartaric and Citric Acids. If a solution of citric acid be colored by addition of one drop of potassium chromate solution, the color, even after addition of a few drops of sulphuric acid does not change on several days' standing. Tartaric acid under similar conditions, especially on addition of sulphuric acid, more or less rapidly according to quantity present, changes to the violet color of the sesqui salts of chromium, and it is possible to positively detect $\frac{1}{2}$ per cent. tartaric acid in citric acid by allowing the time of observation to extend to a few hours. Salzer, in *Berichte*, 1888, p. 1910.

The examination of *belladonna*, *hyoscyamus* and *stramonium extracts* of the various pharmacopœias is tabularized at the conclusion of the various articles by Richard Kordes in the *Pharm. Ztschr. f. Russl.*, 1888, pp. 386, 404, 422.

The extracts were prepared from the same lot of drugs by the author, except in a few cases when the preparation was made from the fresh drug; such preparations were purchased of Merck. The extracts were mixed with lime and extracted with ether; this solution evaporated nearly to dryness and titrated with $\frac{1}{100}$ normal sulphuric acid; on obtaining a faint acid reaction, ether was added to dissolve the resinous matter precipitated, carrying with it a portion of the alkaloid; this precaution was repeated until a permanent slight acid reaction was gotten.

BELLADONNA EXTRACTS—LEAVES.

| AUTHORITY. | Yield of Extr. from drug. | Solid mat- ter in Ex- tract. | Percentage of alkaloid calculated for | | | Percent- age of ex- tracted alkaloid. |
|--------------------------|---------------------------------|------------------------------------|---------------------------------------|-----------|--------|--|
| | | | Normal Extract. | Dry Extr. | Drug. | |
| Fol. Belladonnæ... | | | | | 0.6406 | 100.0 |
| Germ. (Merck)... { | 3.5 to 4% fresh leaves | 78.1% | 1.2056 | 1.5430 | | |
| Neerl., aq. (Merck)..... | | 75.0 | 0.5296 | 0.7056 | | |
| Ross, aq. spir..... | 12.0 | 68.3 | 2.1673 | 3.1730 | 0.2600 | 40.5 |
| Fennic., spir..... | 19.0 | 76.4 | 2.2252 | 2.9425 | 0.4270 | 66.6 |
| Helvet., "..... | 29.2 | 76. | 1.8580 | 2.4430 | 0.5425 | 84.6 |
| U. S., "..... | 15.5 | | 4.0500 | | 0.6277 | 97.7 |
| Internat., "..... | 33.7 | 71.6 | 1.5678 | 2.1890 | 0.6383 | 99.6 |
| Fennic., sic..... | 57.0 | 100.0 | 0.7374 | 0.7374 | | |
| Helvet., "..... | 87.6 | 100.0 | 0.4142 | 0.4142 | | |
| Ross, "..... | 24.0 | 100.0 | 1.0211 | 1.0211 | | |

ROOT.

| | | | | | | |
|--------------------|------|------|--------|--------|--------|-------|
| Rad. Belladonna... | | | | | 0.7398 | 100.0 |
| Austr., spir..... | 25.5 | 66.3 | 2.6828 | 4.0464 | 0.6840 | 92.4 |
| Brittan., "..... | 27.0 | 66.4 | 2.7212 | 4.0982 | 0.7347 | 99.3 |
| Gallic., "..... | 23.0 | 79.5 | 2.6920 | 3.3860 | 0.6278 | 84.8 |
| Internat. "..... | 29.3 | 68.5 | 2.5120 | 3.6060 | 0.7360 | 99.1 |

HYOSCYAMUS EXTRACTS—LEAVES.

| | | | | | | |
|--------------------|------------------------|--------|--------|--------|---------|-------|
| Fol. Hyoscyam..... | | | | | 0.14965 | 100.0 |
| Germ. (Merck)... { | 2.5 to 3 fresh drug | 76.50 | 0.6253 | 0.8043 | | |
| Neerl. "..... | | 77.05 | 0.5032 | 0.6532 | | |
| Austr. "..... | | 76.65 | 0.7027 | 0.9167 | | |
| Ross..... | 10.7 | 66.65 | 0.7270 | 1.0907 | 0.07780 | 52.0 |
| Fennic..... | 20.0 | 79.60 | 0.5123 | 0.6436 | 0.10250 | 68.0 |
| Helvet..... | 18.6 | 76.15 | 0.5390 | 0.7078 | 0.09390 | 62.7 |
| U. S..... | 15.0 | 73.60 | 0.9472 | 1.2860 | 0.14208 | 94.9 |
| Internat..... | 20.6 | 75.20 | 0.6909 | 0.9187 | 0.14230 | 95.0 |
| U. S., fluid..... | 94.5 | 18.05 | 0.1567 | 0.8705 | 0.14808 | 99.0 |
| Helv., sic..... | 55.8 | 100.00 | 0.1203 | 0.1203 | | |
| Ross, sic..... | 21.4 | 100.00 | 0.3338 | 0.3338 | | |

SEEDS.

| | | | | | | |
|----------------------------------|---|-------|--------|-------|--------|-------|
| Sem. Hyoscyam ¹ | | | | | 0.1335 | 100.0 |
| Gallic..... | 7 | 71.85 | 1.3591 | 1.893 | 0.0951 | 71.2 |

¹ Hyoscyamus acid yielded 28.0 per cent., and stramonium seed 28.6 per cent. oil to petroleum spirit.

STRAMONIUM EXTRACTS—LEAVES.

| | | | | | | |
|---------------------|-------|-------|--------|--------|--------|-------|
| Fol. Stramon..... | | | | | 0.2044 | 100.0 |
| Neerl. (Merck)..... | | 77.00 | 0.8718 | 1.1220 | | |
| Ross..... | 12.0 | 74.35 | 0.7120 | 0.9570 | 0.0890 | 43.5 |
| Helv..... | 22.3 | 72.55 | 0.6308 | 0.8694 | 0.1396 | 68.2 |
| Internat..... | 28.4 | 78.00 | 0.7128 | 0.9136 | 0.2024 | 99.0 |

SEEDS.

| | | | | | | |
|---------------------------------|-------|-------|--------|--------|--------|-------|
| Sem. Stramon ¹ | | | | | 0.1510 | 100.0 |
| Fennic..... | 7.5 | 76.25 | 1.6858 | 2.2108 | 0.1264 | 83.7 |
| Gallic..... | 5.0 | 82.30 | 2.5720 | 3.1250 | 0.1265 | 83.7 |
| Internat..... | 7.6 | 74.80 | 1.8640 | 2.4906 | 0.1416 | 93.8 |
| U. S., fluid..... | 87.1 | 6.50 | 0.1679 | 2.5829 | 0.1498 | 99.1 |

Oil of Cajeput is similar in composition to oil of eucalyptus, the examined specimen was *lævogyre*, sp. gr. 0.934, crystallized at -50° C. the crystals melting at -8° C. Subjected to fractional distillation between 70° – 100° , aldehydes were obtained of which butyr- and valer-aldehydes were isolated; at 155° a small portion of a *lævogyre* hydrocarbon $C_{10}H_{16}$ of the terpene series passed over, this formed the derivative $C_{10}H_{17}Cl$; at 165° benzaldehyde was found; between 175° – 180° (representing two-thirds of the oil) *cajeputol*, identical with *eucalyptol* distilled over. Above 180° the distillation was carried on under reduced pressure (0.04 m.) but only small fractions were obtained. Between 130° – 140° a *terpilenol* which after purification crystallizes at -15° on introduction of a small crystal; it has the sp. gr. 0.947 and forms $C_{10}H_{16} \cdot 2 HCl$. This *terpilenol* is identical with the monatomic alcohols (isomers of the borneols) $C_{10}H_{18}O$ which have been obtained by hydration of *terpilene*. The higher fractions contain the acetate, butyrate and valerianate of the *terpilenol*; a body $C_{15}H_{24}$ boiling at 160° closely related to the hydrocarbon of the oils of *copaiba* and *cubeb*; polymers of C_6H_8 with products of oxidation.—*R. Voiry, Chem. Ztg. Rept.*, 1888, 186.

Sulpho-Carbolic Acid has been proven superior to carbolic acid as a disinfecting agent; it appears in the German market as "Roth's Desinfektions-Pulver" made by mixing the acid with infusorial earth first treated with a slight excess of H_2SO_4 to unite with the bases. This contains 14 per cent. of the sulpho carbolic acid.—*Pharm. Ztg.*, 1888, 412.

¹ *Hyoscyamus* seed yielded 28.0 per cent., and *stramonium* seed 26.6 per cent. oil to petroleum spirit.

Glycerin and borax.—The effervescence caused on admixture of glycerin, borax or boric acid and sodium bicarbonate or carbonate has led Dr. Carl Jehn to make some experiments, the results of which show that not only glycerin but all polyatomic alcohols and aldehydes containing as many hydroxyl groups as there are carbon atoms in the formula will do the same. So erythrite $C_4H_{10}O_4$, mannite $C_6H_{14}O_6$, melampyrite (dulcite) $C_6H_{14}O_6$ as alcohols, and glucose, lævulose and galactose, $C_6H_{12}O_6$ as aldehydes will give the reaction. Quercite $C_6H_{12}O_5$, saccharose and lactose $C_{12}H_{22}O_{11}$, and glycogen $C_6H_{10}O_5$ did not start the reaction. An explanation of the reaction is not offered. See paper by W. R. Dunstan, in AMER. JOUR. PHARM., 1883, 447-456. *Arch. Pharm.*, 1888, 495.

Creasote is best administered by mixing with considerable cacao-butter, to absorb the creasote completely, and making into pills. —*Rundsch.*, 1888, 555.

✓ **Cantharidal Camphor-Chloral** proposed as a substitute for cantharidal collodion by Boni (*Arch. de Pharm.*), is prepared of camphor 20; chloral-hydrate 30; powdered cantharides 10. Melt the camphor and chloral by heating to 60° , add the cantharides and, with constant stirring, maintain for some time at 60° - 70° . Filter and preserve in closely stopped bottles.—*Pharm. Ztg.*, 1888, 421.

Powdered Rosin.—H. Hager in *Pharm. Ztg.*, 1888, p. 420, calls attention to the liability to spontaneous combustion of this article. In the case mentioned sufficient heat had been generated to cause the greater part of the powder to reform a solid mass, although the temperature of the room was only 18° - 19° C.

A. Reinhardt, page 437 of *Pharm. Ztg.*, records a similar case. It is advisable to keep the powder in tin boxes with tight fitting covers, so as to prevent as much as possible contact with the air, oxidation being the cause of the rise in temperature.

Lycopodium examined by Langer, contains moisture, 7 per cent.; ash, 1.15 per cent., chiefly phosphates; cane sugar, 2.1 per cent.; nitrogen, 0.857 per cent.; fixed oil, 49.34 per cent., which when fresh is neutral, easily becoming acid, composed of 80 to 86 per cent. *a*-decyl-*b* isopropylacrylic acid with possibly a little myristic acid, glycerin, 2.8 to 5.2 per cent. of the oil. Alcohol macerated with lycopodium at ordinary temperature for 14 days, is oxidized to aldehyde.—*Rdsch.*, 1888, p. 580.

An explosive mixture if not properly compounded: nitric acid, 5.0;

creasote, 2·0; chloroform, 3·0. Due to the chemical reaction of the first two articles which generates such heat that the chloroform boils. Proper procedure: mix the acid and creasote and allow to cool, then add the chloroform.—(*Arch. de Pharm.*) *Pharm. Ztg.*, 1888, p. 442.

Liquor Ferri Albuminati.—100 gm. fresh albumen are mixed with 200 gm. distilled water, strained and the albumen completely precipitated by addition of dialyzed iron, the mixture being constantly stirred. The thick red-brown mixture is passed through a linen strainer until the liquid runs clear, after which it is washed with distilled water until the washings show no reaction with silver nitrate. The strainer, with precipitate, is placed in a tared porcelain capsule with some water, and solution of soda added until the precipitate dissolves, (best ascertained by removing a small quantity in a test tube and noting the transparency), the strainer is then removed and distilled water added to make 700 gm., to which solution is added 100 gm. glycerin, 200 gm. alcohol and any aromatic as flavor.

This solution contains 10 per cent. of ferric albuminate (= 0·65 per cent. ferric oxide), is of alkaline reaction, permanent, easily miscible with fresh and boiled milk, and is not itself changed on boiling. Dose: a teaspoonful two or three times a day, one-half hour before meals.—Köhler, *Schw. Wochenschr. f. Pharm.*, 1888, p. 219.

Tests for Carbohydrates.—Undoubtedly the furfural reactions furnish the most delicate tests for the carbohydrates. H. Schiff uses a test paper made by immersing paper in a mixture of equal volumes of xylinin and glacial acetic acid diluted with alcohol and drying. A small quantity of the substance to be tested is heated with a slight excess of concentrated sulphuric acid and the test paper held in the evolved vapors, a beautiful red color is produced owing to the formation of the furoxylinin. It will detect as little as 0·00007 gm. glucose in an aqueous solution. The author uses a furfural reaction, even more delicate than the above, detecting 0·000028 gm. glucose in solution. One drop of a dilute solution to be tested is mixed with two drops of a 15 per cent. alcoholic solution of α -naphthol in a test tube and $\frac{1}{2}$ cc. concentrated sulphuric acid is carefully poured in to form a distinct layer. If at the line of contact a *violet color* above a green layer is produced, carbohydrates are present. Urine is diluted with 9 volumes of water and *one drop* proceeded with as above. If the violet color is not produced, the urine is considered normal; if the color is produced, the urine may be considered abnormal because it

yields a quantity of furfural which is also obtained from a glucose solution containing at least 0.5 per cent.

By means of these two tests carbohydrates were detected in all urines examined; albumen perfectly free from carbohydrates heated with concentrated acids formed furfural which was recognized in the distillates, establishing for the first time by chemical reactions a close relationship between the albuminoids and the carbohydrates.

In testing urine for carbohydrates, if albumen be present in larger quantities it must first be removed, small quantities do not introduce appreciable errors, owing to the small quantity of urine taken. Fehling's solution under the most favorable conditions failed to detect less than 0.00012 gm. glucose in aqueous solution; testing urine by the three tests the bodies other than carbohydrates decrease the delicacy of Fehling's test to a greater degree than the first two tests.—*Dr. L. v Udránszky, Zeitschr. f. Phys. Chem., May 1888.*

NOTES ON EAST INDIAN GUMS.

By J. G. PREBBLE, BOMBAY.

During the last few years large quantities of gums, the production of Indian trees, have been exported from Bombay. About three-fourths of these exports go to the United Kingdom, and always I think to London, under the names of "ghátí," "amrad," "oomra-wutty," etc. In a recent paper on these gums, published in this Journal,¹ these names and the origin of the gums do not appear to be well understood. Hence some notes on these points may be of interest.

"Ghátí," an aboriginal or purely Indian word, has the primary meaning of a strait or pass through a mountain. Drugs or vegetables of country or local production are sometimes distinguished as "ghátí" from those which are imported from foreign ports or from a distance; thus there is "ghátí-pitpapra" (*Justicia procumbens*), which is used as a substitute for the true pitpapra (*Fumaria officinalis*), imported from Persia, and "ghátí-mirchi" (*Capsicum annuum*), country-grown chillies, as distinguished from a variety resembling the West Indian and imported from Goa and known as "gowar-mirchi,"² and lastly

¹ "Ghatti and other Indian Substitutes for Gum Arabic," *Pharm. Journ.*, April 14, 1888; *AMER. JOUR. PHAR.*, June, p. 301.

² Dymock, "Materia Medica of Western India."

"ghátí gum, gum collected on the ghats and hills of the country and called "ghátí" in contradistinction to the variety imported from foreign ports.

The best picked "ghátí" gum as now exported from Bombay is entirely or almost entirely derived from *Anogeissus latifolia*.¹ I think Dalzell is the first author who mentions this gum. He says, "the tree produces a very white, hard and valuable gum." The Bombay name is "daura" or "dabria." It is largely used throughout India for calico printing, for which it has a high reputation, and as has been shown by Mander it may with advantage be used in pharmacy in place of the high priced and scarce Kordofan gum. I have obtained the same reactions with this gum as was observed by Mander with a London sample of "ghátí" gum, hence I conclude that his sample was free from admixture with other gums.

"Oomrawuttee gum derives its name from Oomrawuttee, or Amravti, the chief town of the Hyderabad assigned districts known as the Berars, the centre of a prosperous trade and officially described as "the very home of the cotton plant and the heart of the cotton trade in India." It gives its name to a variety of cotton staple, "the Oomrawutties," and such phrases as "good oomras," "good fine oomras," "oomra variety," are to be met with in the Bombay cotton market reports. Oomrawutti gum is considered by the native gum dealers in Bombay to be of two kinds, the "ghátí" and the "amrad;" the latter they consider to be derived from the babool tree (*Acacia arabica*). Babool gum is distinguished from all other gums that I have examined by being unaffected by either neutral or basic acetate of lead, and by being more or less darkened, but not gelatinized, by ferric chloride. Samples of babool gum that have hung long on the tree and are of a deep reddish-brown color give a very dark coloration, almost black, but the pale samples are less affected. The Oomrawuttee sample examined by Mander was evidently babool gum. With regard to the name "amrad," I do not think it has any reference to "amra," the native name for the gum derived from *Spondias mangifera*, as this gum has a character more nearly resembling tragacanth than arabic gum. Forty grains of it form a jelly with about two ounces of water. I thought it might be a corruption of "amravti," but the gum dealers can give no satisfac-

¹ I consulted Dr. Dymock on this point, and he is also of opinion that the gum now exported as ghatti is derived as stated.

tory explanation of the meaning of the word further than that it is applied to all gums of a reddish tint. It is therefore probably a word imported into India, and as the name is principally applied to Barbary and Egyptian gums it may be a corruption of the Arabic word *hamrā*, red, and this thought is supported by a statement I have recently seen that "amrad" is a corruption of "amhara,"¹ a name applied to a gum derived from an acacia.

Gums are sent to Bombay from all parts of India, but the best come from Amravti. Other centres are Nagpur, Jubbnepur and Cawnpur, and a good deal is collected on the ghats of the Bombay presidency. On arrival in Bombay they are sorted by Cooly women and children. Anogeissus gum, possessing well-marked physical characters, is easily separated, and is sent to the London market almost free from admixture, but the dark colored or amrad gums are generally mixtures of various gums, babool gum predominating. During the last financial year 20,895 cwts. of gum arabic of Indian production were exported from Bombay, valued at R7,93,934.²—*Phar. Jour. and Trans.* July 7, 1888.

NOTES ON SENNA.³

BY CHARLES HEISCH, F.I.C.

Having had some samples of powdered senna brought to me by one of my inspectors, I was somewhat puzzled what to do with them. Not only was it possible that other leaves might be powdered with the senna, but that exhausted leaves might be also added. Many varieties of cassia appear to be sometimes found mixed with senna, and so long as you have the leaves you can mostly detect them, but when powdered you lose the characteristic appearances.

The principal adulterants of which I can find any account are *cynanchum argel* and *coriaria myrtifolia*, the latter being a poisonous plant used by dyers and tanners, sometimes called tanners' sumac.

How argel is to be detected in powdered senna, I cannot at present say; I have not yet got a specimen. Fortunately the worst adulterant

¹ *British and Colonial Druggist*, May, 19, p. 536.

² "Annual Statement of the Trade and Navigation of the Port of Bombay," 1886 and 1887.

³ Read at Meeting of Public Analysts, June, 1888. Reprinted from *The Analyst*, August.

—the *coriaria myrtifolia* gives when infused precipitates with gelatin, bichloride of mercury, and antim. tart. which senna does not, and also a dark blue with salts of iron. The only bad case of adulteration which I have met with was with buchu leaves. These would have attracted the attention of anyone on the look out, by their different shape and peculiar odor, but in the case referred to did not attract the attention of the purchaser, who made his senna tea, and suffered accordingly. Had the sample been in powder, the mistake would have been almost unavoidable. As partially exhausted leaves would, of course, give less ash and extract than the senna unexhausted, I made some examinations of undoubtedly pure senna leaves, both Alexandrian and Tinnevely, and though the results show nothing very striking, I think they are of sufficient interest as a small contribution to our knowledge to be worth laying before you.

| No. | Kind and Source. | Total. | Sol. in Water | Sol. in HCl. | Insoluble. | Alkalinity as K_2O | Alcoholic Extract of Ash & Water-free. |
|-----|---|--------|---------------|--------------|------------|----------------------|--|
| 1 | Tinnevely, Brown and Smart | 11.48 | 2.4 | 8.86 | .2 | 1.16 | 30 |
| 2 | Same powdered..... | 11.22 | 2.31 | 8.77 | .1 | 1.14 | 29.9 |
| 3 | Tinnevely, Apothecaries' Hall | 11.34 | 2.35 | 8.72 | .2 | 1.16 | 33.19 |
| 4 | Same powdered..... | 11.39 | 2.67 | 8.31 | .4 | 1.06 | 31.78 |
| 5 | Powdered Alexandrian, Brown and Smart..... | 11.69 | 2.35 | 7.86 | 1.49 | .84 | 33.3 |
| 6 | Alexandrian Apothecaries' Hall | 11.64 | 2.91 | 8.36 | .37 | 1.06 | 29.04 |
| 7 | Ditto in powder..... | 11.35 | 2.66 | 7.98 | .60 | 2.06 | 30.13 |
| 8 | Alexandrian, Allen and Hanbury | 12.36 | 2.96 | 9.02 | .38 | 1.54 | 35.5 |
| 9 | Same powdered..... | 12.54 | 3.18 | 9.12 | .24 | 1.76 | 35.41 |
| 10 | Powder from Allen and Hanbury, believed to be mixed | 13.98 | 1.22 | 11.91 | .85 | 1.69 | 27.75 |
| 11 | Powder No. 85, from Hampstead | 19.01 | 3.01 | 12.86 | 3.14 | 1.22 | 29.55 |
| | Ditto No. 88, ditto..... | 12.89 | 2.48 | 9.05 | 1.36 | 1.25 | 30.00 |
| 12 | Buchu leaves..... | 6.06 | 2.73 | 3.25 | 0.07 | 1.47 | 17.49 |

On examining powdered senna under the microscope, one is struck by the fact that the white translucent hairs from the back of the leaf are quite unchanged by the powdering, so that if one is familiar with the appearance of undoubtedly genuine samples of powdered senna

one can get an idea if any other samples contain about the right quantity of hair, which is some guide. I then took the ash in dried samples of the leaves; the amount soluble in water and its alkalinity; the amount sol. in HCl and the insoluble; and, finally, the amount of alcoholic extract calculated on the ash and water-free leaves. The results are contained in the accompanying table.¹

It will be observed that the samples obtained from Messrs. Allen and Hanbury contain considerably more ash than the others, and with one exception yield more extract. I have added the results obtained from the two District samples of powder, which in point of extract closely resemble the majority, but one of them differs largely in ash. I have also added the results obtained from buchu leaves, which give about half, both ash and extract.

A NEW BASE IN TEA.²

BY A. KOSSEL.

In the examination of large quantities of tea extract received from Dr. Fr. Witte, of Rostock, I have ascertained the presence of a new base that is associated with theine in minute proportion. The syrupy extract was operated upon in the following manner: After mixing with water sulphuric acid was added to separate smeary products, and the resulting liquid was supersaturated with ammonia. Ammoniacal solution of silver nitrate was then added, and the precipitate thus formed was collected by filtration. The precipitate was digested with warm nitric acid, the mixture filtered to separate silver salts that had deposited, and the filtrate made alkaline with ammonia. In the course of twenty-four hours a brownish amorphous precipitate was deposited, which contained the new base in the state of a silver compound, and by evaporating the clear filtered liquid a further quantity of this silver compound was obtained. After separating the silver from this compound by treatment with sulphuretted hydrogen and filtering, a

¹ It will be observed that several are done in duplicate, one on the leaf whole and the other on the powdered leaf. I thought it just possible the results might differ, as in the powder the proportion of veins from the leaves might be differently distributed. When bought powdered, the samples mostly contained more ash.

² *Berichte der deutschen chemischen Gesellschaft*, 1888, No. 11, p. 2164; reprinted from *Pharmaceutical Journal and Transactions*, July 21.

small quantity of xanthine was deposited from the clear filtrate,¹ and upon concentrating the liquid the new base partly crystallized out. The mother-liquor was then mixed with mercuric nitrate solution, the precipitate collected by filtration, and the filtrate made alkaline with sodic carbonate solution. A white precipitate was thus obtained in both cases, which consisted almost entirely of a mercury compound of the base.

Analysis of the new base, for which I suggest the name "theophylline," gave the following results :

| | I. | II. | III. | Calculated for $C_7H_8N_4O_2$. |
|-------|-------|-------|-------|------------------------------------|
| C . . | 46.55 | 46.63 | — | 46.67 |
| H . . | 4.70 | 4.77 | — | 4.44 |
| N . . | — | — | 31.66 | 31.11 |

The crystals contain one molecule of water, which is given off by heating to 110° C.

The composition of theophylline is the same as that of theobromine, as well as that of paraxanthine obtained by Thudichum and Salomon from urine, but the characters of the base are different from those of either substance. The crystals are larger than those of theobromine, and the latter do not contain water. Theophylline is much more soluble in water than theobromine, and on the addition of a very small quantity of ammonia it dissolves very readily apparently in any proportion, while theobromine is but sparingly soluble in strongly ammoniacal water. The crystals of paraxanthine have been examined by Arzruni, and Dr. Scheibe has compared the crystals of theophylline with his description, with the result that they do not correspond. The melting point of theophylline is about 264° C., while that of paraxanthine obtained from Dr. Salomon is 280°.

¹The occurrence of xanthine in tea was ascertained some four years ago by Dr. Adolph Baginsky, who undertook the search for it at the suggestion of Dr. Kossel (*Zeits. f. Physiol. Chemie*, viii., 395). For that purpose tea was extracted with dilute sulphuric acid, the clear liquor mixed with excess of baryta water and then treated with carbonic acid to remove the excess of baryta. After filtering and evaporating, ammonia and silver nitrate were added, and the precipitate of xanthine silver thus obtained, crystallized from solution in dilute nitric acid mixed with some urea. This salt contained 33.6 per cent. of silver, very nearly the amount required by the formula $C_5H_4N_4O_2AgNO_3$. The quantity of the silver compound obtained from one pound of tea was only 0.1567 gram.—*Ed. Pharm. Journ.*

Theobromine sublims at 290° C. without melting. Theophylline also sublims at a temperature above its melting point.

Theophylline forms definitely crystallizable salts with hydrochloric and nitric acids, platinum chloride and gold chloride, as well as a crystallizable sparingly soluble double salt with mercuric chloride. In a pure state the base is not precipitated from a dilute solution by mercuric nitrate.

Paraxanthine forms, as Salomon showed, a sparingly soluble compound with soda, which separates in crystals on adding caustic soda solution to a dilute solution of the base. Theophylline also forms a compound with soda, but it is readily soluble, this difference between the two bases being very marked.

Theophylline resembles theobromine in forming a silver compound which separates in an amorphous state on adding silver nitrate to a water solution of the base. This compound is soluble in warm ammonia, and on cooling the solution it crystallizes out. The compound thus obtained and dried at 130° C. contained 37.18 per cent. of silver, corresponding to the formula $C_7H_7N_4O_2Ag$. This silver compound dissolves readily in nitric acid.

When theophylline is mixed with chlorine water and the liquid evaporated, a scarlet-colored residue is left, which becomes violet on addition of ammonia, just as is the case with theobromine.

The great similarity between the characters of theophylline and theobromine suggest that these substances are both derivatives of xanthine, and with that idea the introduction of the methyl group was attempted. By heating the silver compound with a calculated proportion of methyl iodide and some methyl alcohol in a closed tube for twenty-four hours at a temperature of 100° C. a crystallizable product was obtained which showed on analysis that a methyl group had been taken up, the composition and characters agreeing perfectly with those of caffeine. The melting point of the substance thus obtained was 229° C., and accordingly from this experiment it may be inferred that theophylline is a dimethylxanthine. The positions of the methyl groups have yet to be determined by an oxidation experiment.

NOTE.—Theophylline is doubtless the same base which in 1871 was obtained in small quantity by Zoeller (*Annalen*, vol. 158, p. 185) from Himalayan tea, and which Liebig believed to be identical with theobromine, mainly because it yielded a crystallizable silver com-

pound. A second base has also been observed by Paul and Cownley shortly after the publication of their paper, "Chemical Notes on Tea," (*AMER. JOUR. PHAR.*, 1887, p. 626); the acid liquid from which the theine had been removed by chloroform, was rendered alkaline by potassa, and again shaken with chloroform, when a very small quantity of alkaloid was obtained, apparently amorphous, insoluble in hot water, but soluble in ether, and therefore differing from both theine and theobromine (*Phar. Jour. and Trans.*, July 14, 1888, p. 24).—
EDITOR *AM. JOUR. PHAR.*

PEPSIN.

BY A. PERCY SMITH, F.I.C., F.C.S., RUGBY.

The method usually adopted for estimating the peptonising power of pepsina porci consists in dissolving 1 to 2 grains in 8 to 12 ounces of water, to which 40 to 60 minims of hydrochloric acid has been added. 500 to 1000 grains of hard-boiled white of egg, granulated by rubbing through a wire sieve, is immersed in the liquid, and the whole kept at 98° to 130° F. for four hours, when the undissolved albumen is filtered off through muslin, and, after partial drying, is weighed to ascertain the amount dissolved. The variable numbers above quoted embrace various formulæ recommended by different experimenters.

This method of analysis is excessively crude and untrustworthy. When hard-boiled white of egg is kept in warm water it absorbs a considerable quantity of that menstruum, as much as several units per cent.; consequently, on weighing the residual albumen, you may find that the weight is greater, instead of less than that with which you started, the gain in weight due to absorbed water more than counterbalancing the loss obtaining through solution, as has happened with indifferent samples of pepsin. Then who shall say when, by simple air drying, the albumen has regained its former condition? The enormous quantity of albumen is foreign to the usual habits of the scientific analyst, and involves an enormous waste of time in manipulation.

One trial of this method was enough for me. The first modification I adopted consisted in substituting for the large quantity of granulated albumen a single half of the white of an egg in one piece. I likewise arranged a check experiment in which the pepsin was omitted, other conditions remaining unaltered. At the end of four hours the residual

pieces of albumen were placed on blotting-paper to remove superfluous moisture, and weighed. The gain in weight of the albumen in the check experiment, due to absorbed water, was calculated into percentage, and the same deducted from the weights of the other portions which had been subjected to the action of various pepsins. This, although an improvement upon the old method, proved likewise unreliable, because the water absorbed was not equal in each experiment. The albumen which was immersed in acidulated water only quickly dried, superficially, when placed on blotting-paper, whereas that which had been acted on by pepsin was rendered glutinous and incapable of being dried in this manner. In fact one sample weighed considerably more than it did at starting, even after deducting the allowance for water absorbed.

I next tried much smaller pieces of albumen, about 1 cc., in hope that complete solution might ensue, and a time value be obtained. I soon found, however, that the solubility does not depend upon the mass, but upon the surface exposed.

Finally I discarded altogether the use of fresh white of egg, and had recourse to dry powdered albumen, prepared by drying in a steam oven and levigation in a mortar. With this I succeeded in getting accurate comparisons between the digestive powers of various pepsins. Albumen in this form dissolves with rapidity, owing to its state of fine division. Any remaining undissolved can be filtered off on a counterpoised filter paper, and heated in a water oven until absolutely dry. It is, however, unnecessary to do this when two samples only are compared against each other, nor is it essential to know the actual weight of albumen employed, provided it be the same in each experiment. This is ensured by placing some on the naked pan of the balance (there is no objection to so doing, as it is a dry gritty powder, and does not adhere to the metal), and counterpoising by a similar addition to the other pan.

Let the albumen fall on the centre of the filtered liquid, avoiding, if possible, contact with the glass of the beaker. It soon sinks, and after the lapse of some time, a simple inspection will show which is dissolving with the greater rapidity. Agitation assists solution, therefore take the two beakers, one in each hand, and rotate the contents equally. When one sample has dissolved all the albumen it is manifestly superior to the other which has failed to do so in the given time. If many samples have to be compared it will be necessary to start with

known quantities of albumen, and weigh the undissolved residues in the manner above indicated.

An objection may possibly be raised to this modified method, viz., that albumen as ingested is not in the form of a dry powder, and that we ought to copy as nearly as possible the conditions existing in the stomach. To this I would reply that it does not matter in the least, to us, as analysts, what are the conditions which obtain in the stomach; since there is no absolute test for pepsin, we can only compare one sample against another, and that which dissolves the most albumen in the shortest time is taken to be the best.

Another imperfect method of analysis is that employed in the examination of malt extracts for diastase; in which a certain weight of extract ought to dissolve a certain weight of starch in ten minutes, when if it does so dissolve it, the extract is a good one, if not it is to be condemned. The more correct way is to ascertain the reducing power on Fehling's solution, before and after digestion with an *excess* of starch, and I intend to say a few words upon this subject on a future occasion, when I have ascertained the maximum amount of diastase existing in the best samples of malt.—*The Analyst*, Aug. 1888.

RELATIVE VALUE OF DIFFERENT PEPSIN TESTS.¹

BY JAMES H. STEBBINS, JR.

The methods I propose to discuss in this paper are three, viz.: the U. S. P. test, the Manwaring test and the Kremel test.

According to the experiments of numerous investigators, the peptic digestion of albuminoids depends upon several conditions.

1. The temperature.

The pepsin of fish acts energetically at 20° C., but the pepsin of mammals requires a higher temperature, and it has been found that peptonization is most active between 35° C.—50° C. Above this, digestion runs much slower and ceases totally towards 70–80° C.

2. The quantity of pepsin.

There being no such thing as absolutely pure pepsin, it has been impossible to determine, with accuracy, the amount of albumen which can be converted into peptone by a given quantity of the ferment.

¹ Abstract from a paper in *Journal of the American Chemical Society*, March, 1888.

We know only that the amount is very large, provided that from time to time a little acid and water is added in order to maintain a certain degree of dilution.

The quantity of albuminoid which can be digested in a given time increases rapidly with the quantity of pepsin employed till it reaches a maximum, and then decreases slowly. The quantity of peptone finally obtained increases with the proportion of pepsin.

3. The quantity of water.

As the products of digestion accumulate, the rate of peptonization gradually decreases. The addition of a fresh quantity of acidulated water causes the peptic action to recommence until it has reached a certain limit, beyond which the reaction ceases entirely.

4. The nature and quantity of the acid used.

A large number of acids may take the place of hydrochloric acid in peptic digestions, but none of them are as efficient as the latter. A. Mayer found that with the use of hydrochloric acid, complete peptonization occurred in from 3 to 5 hours; with nitric acid in about 5 hours, with oxalic acid in 13 hours, and with sulphuric acid in 19 hours.

According to Brücke, peptonization is already very active in a medium containing only 0.8 parts of hydrochloric acid per 1,000, and attains its maximum, with a concentration of 1 pt. of acid in 1,000 of water. A too large proportion of acid hinders peptonization, 7 pts. of acid per 1000 of water being sufficient to make the action very slow. Mayer thinks that the most favorable proportion of acid is 2 pts. per 1,000 water, or 0.2 per cent.

5. The time of action.

6. The variety and character of the albumen.

One of the most largely used tests in this country is the U. S. P. test, which reads as follows:

"One pt. of saccharated pepsin dissolved in 500 pts. of water, acidulated with 7.5 pts. of hydrochloric acid, should digest at least 50 pts. of hard boiled egg albumen, in 5 or 6 hours, at 100-104° F. (37.5-40° C.)"

The above test seems simple, but, in reality, it is unreliable and misleading, as no two persons using the same pepsin can obtain the same or even approximate results; it is, therefore, not surprising that we meet with such a diversity of conclusions.

The weak points in the above test are the following:

1. The test is based upon the amount of albumen which can be dissolved in a given time (including peptone and intermediary products), but does not take into consideration the amount of peptone actually formed, and this I claim to be of the greatest importance.

2. It directs that a given pepsin shall digest at least 50 pts. of coagulated albumen. Now, in order to determine how much albumen has actually been dissolved, it is necessary to use an excess of albumen, and then weigh what remains undissolved. The test in question does not specify how much albumen shall be used, but leaves it entirely to the option of the experimenter. I consider this to be a weak point, as it makes quite a difference whether only a small or large quantity of albumen is used.

3. It is difficult to see how accurate results are to be obtained by weighing the amount of undissolved albumen remaining after a digestion, because it is impossible to find two samples of coagulated albumen, which contain exactly the same quantity of moisture; and besides this, the quantity of moisture is very liable to vary during the weighing, owing to the loss of moisture by evaporation.

4. It is not stated how long the eggs should be boiled. This is a very important matter, as digestion differs greatly according to whether the eggs are boiled for a short or a longer time.

5. No provision is made for the size of the pieces of coagulated albumen. This, also, is very important, as it has been found that the greater the surface of the albumen exposed to the peptic ferment, the greater will be the amount of albumen digested.

6. This test applies only to saccharated pepsins, and no provision is made for other brands of pepsin.

It will, therefore, be seen that the U. S. P. pepsin test is absolutely unreliable and misleading.

Lately my attention has been called to a pepsin test, which I will designate by its author's name, the "Manwaring test." In this test Manwaring has tried to avoid as much as possible the bad points of the U. S. P. test; but in doing this he has stumbled against other sources of error which I will try to make clear further on.

The test can best be described in the words of its author :

"The design of the following mode of testing the dissolving power of pepsin is to conform as nearly as possible to the U. S. P. test, which, contemplating the testing of the saccharated form, makes no provi-

sion for the proportion of acidulated water to be used with a pure pepsin.

"On the basis that 1 part of a pure pepsin is capable of dissolving 1,000 times its weight of coagulated egg albumen in 6 hours, a saccharated pepsin made with a pure pepsin of U. S. P. strength would contain 5 per cent. of pure pepsin; therefore if 1 grain of a U. S. P. *saccharated* pepsin is to be tested in the presence of 500 grains of acidulated water, then 1 grain of a pure pepsin should be tested in the presence of 10,000 grains acidulated water, to equal the same proportion of water and acid used for the *actual* quantity of pure pepsin contained in a U. S. P. saccharated pepsin when tested according to the U. S. P."

In order to render the weighing of small quantities of pure pepsin as easy as possible to the pharmacist, Manwaring recommends that it should be saccharated, and for this purpose he gives the following recipe:

Rx. Saccharated pepsin consisting of:

| | |
|------------------|--------|
| Pure pepsin..... | 1 gm. |
| Milk sugar..... | 19 gm. |

To make the test take of the above saccharated pepsin 0.3 gm. (=0.015 gm. pure pepsin).

| | |
|-----------------------------|----------|
| Coagulated egg albumen..... | 22.5 gm. |
|-----------------------------|----------|

Acidulated water consisting of:

| | | |
|---------------------------------|---------|---------|
| Distilled water 100 cc. | } | 154 cc. |
| Hydrochloric acid U. S. P. 1.25 | | |

The eggs are to be boiled for 15 minutes and the whites pressed (by means of a spatula) through a (preferably flat) 30 mesh sieve. For the sake of uniformity, the egg whites should be cut into small pieces and thoroughly mixed before being passed through the sieve.

The mixture should be maintained at 100-105° F. for six hours, and agitated thoroughly about every half-hour.

At the end of six hours the temperature of the bath should be quickly run up above 145° F. to destroy the pepsin, then the bath with contained bottles allowed to remain undisturbed over night, that the undissolved albumen may settle.

If the test bottle has been kept securely corked during the test, or

if by previously weighing bottle and contents and afterwards making up with water any loss from evaporation, the quantity of albumen dissolved may be easily determined as follows:

From the settled contents of the test bottle pipette off 10 cc. and evaporate to dryness—until weight is constant—in a watch glass. From this dry residue figure as follows (1 pt. of peptone or intermediate products representing 1 pt. of original albumen):

Suppose 10 cc. of the liquid = 0.2 gm. dry residue; $1\frac{7}{8}$ times its weight = the quantity of water contained in the 10 cc. that was derived from the albumen dissolved; 10 cc. of liquid less 1.4 cc. of water leaves 8.6 cc. water taken from the 154 cc. of acidulated water in making the test.

1.6 grms. or 8 times 0.2 gm. dry residue = the quantity of albumen in its natural state as originally used, that has been dissolved in the 10 cc. of liquid evaporated to dryness.

Therefore, if 8.6 cc. acidulated water holds 1.6 gm. egg-albumen,
then 154 cc. " " " 28.5 " "

Then, as 0.015 gm. pepsin dissolved 28.5 gms. coagulated egg-albumen, 1 pt. would dissolve 1900 times its weight.

The use of the multiplier 7 and 8 is based on the fact that egg-albumen averages $12\frac{1}{2}$ per cent. or $\frac{1}{8}$ dry.

As will be seen, this test is quite a departure from the U. S. P. test, and in some respects is an improvement upon the latter, but I object to it on several points, viz.:

1. It makes no provision for other than concentrated, or, as Manwaring calls them, *pure* pepsins, while in reality the number of these is small compared to the saccharated pepsins.

2. The peptic principle is not killed at 145° F. = 62.2° C.; but digestion may and does continue up to 80° C.

3. Of the undigested albumen remaining in the test bottle, a little remains suspended in the liquid, is pipetted off and adds to the weight of the dry residue.

4. On evaporating the 10 cc. to dryness the residue chars owing to the free H Cl present.

5. The residue, not charred, is a mixture of undigested albumen, partly digested albumen and fully digested albumen or peptone. Peptone only being assimilable in the human system—not the intermediary products—the amount of true peptone formed indicates the strength of the pepsin.

6. The accuracy of the multipliers 7 and 8 is not infallible in every test.

As Manwaring lays particular stress upon the question of dilution, I think his test is a decided improvement over the U. S. P. test.

The next good point in his test lies in the fact that he does not attempt to weigh the undigested albumen, as is done in the U. S. P. test, and thereby does away with a great source of error; but instead of this he figures the amount of albumen (?) digested upon a dry basis, and then tries to convert this dry basis by calculation into albumen on the wet basis. In doing this errors are apt to occur as I have pointed out, but I do not think that they are errors of such magnitude as are apt to be obtained with the U. S. P. test.

Finally, I wish to say a few words about a test which I consider to be the only approach to an accurate method of testing pepsin that I know of. I do not claim that this test is absolutely accurate either, as slight errors are apt to occur, which, however, do not materially injure the final result. I refer to the Kremel test, which was published some time since in the Druggists' Circular.

In devising this test Kremel has made a radical departure from the usual methods, and bases his test upon the fact that under the conditions in which artificial peptic digestions take place, pepsin alone has the property of converting albuminoid matter into peptone, and that, therefore, from an analytical as well as from a physiological standpoint, the only correct method is to take the quantity of peptone produced as a gauge of the action of the pepsin; or in other words, the test is made to resemble as nearly as possible the conditions existing in the natural process.

Without going into any further detail, the test is made as follows:

One gm. of egg albumen (soluble) dried at 40°C. and pulverized, and 0.1 gm. of the pepsin to be tested, are placed into a 100 cc. flask, and dissolved in 50 cc. of 0.2 per cent. hydrochloric acid. The solution is heated to 38–40°C. for three hours, and then exactly neutralized with sodium carbonate; it is then heated on a water bath to 90°C., and cooled after coagulation has taken place. The flask is then filled to the mark with distilled water, and 50 cc. are filtered off and evaporated to dryness in a platinum dish on a water bath.

The residue is dissolved in hot distilled water, filtered through a

moist filter into a platinum dish, and the filter carefully washed. The solution is again evaporated to dryness and weighed. The peptone is then incinerated with ammonium carbonate, and the weight of the ash deducted leaves the weight of the pure peptone, or the representative of the digestive power of the pepsin.

The good qualities of the above test are the following :

1. Simplicity.
2. No guesswork, troublesome calculations or the use of questionable factors.
3. No weighing of albumen dissolved in hydrochloric acid, undigested albumen and intermediary products along with the peptone. This is all obviated by the use of soluble egg albumen, coagulation and filtration or removal of the undigested portion as detailed above.
4. The ease with which it is possible to duplicate and still obtain concordant results.

On the other hand, the objections to this process are the following :

1. The great difficulty of procuring absolutely pure soluble dried egg albumen. This source of error, however, in my opinion, is very slight, because in each test a large excess of albumen is always used, and consequently the pepsin always has enough albumen to act upon. Besides this it must be remembered that only the peptone formed is weighed, and not the amount of undigested albumen, as is the case with the U. S. P. test.

2. It may be objected to this test that the results obtained are expressed by the weight of peptone formed and not by the weight of albumen dissolved, and consequently the figures, being based upon dry peptone, will be much lower than when the result is expressed as so much moist or coagulated albumen. If this, however, be objected to, it is comparatively easy to obtain higher figures by a simple calculation. Assuming that the amount of dry peptone obtained is equivalent to so much dry albumen, then by multiplying the weight of the latter by 8 (Manwaring's multiplier) we would obtain the equivalent in coagulated or moist albumen. I do not think it necessary or advisable to follow this course, as it involves the use of a multiplier which, as already pointed out, is questionable.

3. It takes a little longer to make a test by this process, but if accuracy is thereby gained the process is to be preferred.

To further illustrate the test, I append the following results obtained with commercial pepsins :

| | Peptone formed from 0.1 gm. pepsin in 3 hours. |
|-------------------------------|---|
| Pepsin G..... | 0.5844 |
| " E..... | 0.4972 |
| " B..... | 0.4722 |
| " F, crystal..... | 0.4682 |
| " C (saccharated)..... | 0.4676 |
| " H..... | 0.4598 |
| " A (saccharated?)..... | 0.4370 |
| " A (saccharated)..... | 0.4246 |
| " D plain, soluble..... | 0.3470 |
| " D pure, scales..... | 0.3250 |
| " D pure, another sample..... | 0.3146 |
| " I (saccharated)..... | 0.2780 |
| " J French..... | 0.1848 |
| " K (saccharated)..... | 0.1738 |

These tests were all made with the same quantity of pepsin, whether the latter was saccharated or not, and I think are a fair indication of the relative values of the different pepsins.

It may be objected that this test does not do a concentrated pepsin full justice, on the ground that the latter would form a much greater proportion of peptone and thus retard if not completely arrest any further action of the pepsin upon the albuminoid matter.

In order to test this question, I saccharated samples of E, F and H respectively, according to Manwaring's directions, which is equivalent to diluting with mere acidulated water, and submitted them to the same conditions as before and obtained the following results :

| | Peptone formed from 0.1 gm. pepsin in 3 hours. |
|---------------|---|
| Pepsin E..... | 0.2620 |
| " F..... | 0.1240 |
| " H..... | 0.1250 |

It will be observed that in these tests the figures are considerably lower than in the former ones ; but it must be remembered that the pepsins with which the tests were made were twenty times weaker, or rather more diluted, than in the previous tests, and notwithstanding this the peptone formed is proportionally larger than before. This would clearly show that the dilution is beneficial in the case of concentrated pepsins, as it corrects the retarding action of peptone. As the dilution in these last tests was twenty times greater than in the

previous ones, we ought, by multiplying each of the above results by twenty, to obtain the amount of peptone which would be formed by using the pepsins in their concentrated forms, viz.:

| | |
|---------------|--|
| | Peptone that should be formed from 0.1 gm. concentrated pepsin in 3 hours. |
| Pepsin E..... | 5.240 |
| " F..... | 2.480 |
| " H..... | 2.500 |

The above figures are not, however, obtained as has already been shown, and therefore the calculation is erroneous.

As all the results obtained by strictly following Kremel's directions are comparable among themselves, I do not see how the process can well be improved upon.

The mere fact that increased dilution increases the yield of peptone is not, in my opinion, sufficient reason for condemning the process. As the conditions prevailing in the stomach of a full grown man do not differ materially as to dilution from day to day, it is safe to say that pepsins of varying strength administered to such a person will only perform a certain amount of work and no more, and that, consequently, the results obtained by this test more closely resemble the conditions prevailing inside the stomach than any other.

In conclusion, it will be seen that all the tests mentioned in this paper are subject to faults and imperfections, some having more than others; and, therefore, all we can do under the present unsatisfactory state of affairs is to select the one which is least objectionable, and this, in my opinion, is the Kremel test.

Condurango.—Professor Oser, of Vienna, who has been making trials of condurango bark in carcinoma and other diseases of the stomach, finds that it has an excellent effect on the appetite and that it relieves over-sensitiveness. Some patients can take it for months without any unpleasant symptoms, while in others it soon sets up nausea, which cannot be prevented either by the simultaneous administration of correctives or by the employment of different preparations of the bark, such as the vinum or the liquor. Condurango appears to Professor Oser to deserve a place in our materia medica as a symptomatic remedy, but as to its exerting any specific action on malignant disease, he still holds to his own dictum that the only hope of cure in cancer of the stomach by means of drugs lies in the possibility of a mistaken diagnosis.—*Jour. Am. Med. Assoc.*; *Lancet*, May 19, 1888.

ON THE ANTISEPTIC ACTION OF CHLOROFORM WATER¹.

BY PROF. SALKOWSKI.

The author has investigated, after Koch's methods, the degree to which chloroform water acts upon micro-organisms. He has used chloroform for some years to prevent urine decomposing before he had time to examine it. [I learnt to use it with the same object for albuminous liquids, when in Leipzig in 1882.] Chloroform prevents all fermentations which depend upon the growth of micro-organisms—*e. g.*, alcoholic fermentation, ammoniacal fermentation of urea, conversion of hippuric acid by fermentation into benzoic acid and glyocol, lactic fermentation, and the putrefaction of albumins. But it has no action on those processes caused by unorganized ferments, as ptyalin, pepsin, etc.

Milk, to which has been added a little chloroform, kept in a well-corked bottle, keeps its alkaline reaction, but at the end of three months changes to a fine jelly, which, by shaking, forms a white sediment of casein and fat, and a yellowish clear liquid. Sterilized milk behaves in the same manner, which Meissner explains as due to a slowly acting curdling ferment. Cane-sugar and grape-sugar along with chloroform do not ferment with yeast, but next day the cane-sugar is converted into invert-sugar, by an unorganized ferment in the yeast. Albuminous transudations and pounded meat remain sweet when treated with chloroform, and are found to be free from organisms, both by the microscope and by inoculating gelatin and other nutrient media.

Further, chloroform not only hinders the development of micro-organisms, but also brings about their destruction. Thus a stinking meat broth, shaken up with a few drops of chloroform, at the end of an hour was quite sterile.

Silk threads, impregnated with anthrax-bacilli, free from spores, and exposed to chloroform water for 24 hours, failed to inoculate gelatin plates, etc., whilst in control experiments a positive result was obtained. Mixtures of chloroform water and crushed spleens from cases of splenic fever were found to be sterile after standing 30 minutes. Guinea-pigs were inoculated with half a Pravaz's syringe-full of a fluid, composed of one drop of anthrax blood and 8 cc. of sterilized

¹ *Deutsche medicinische Wochenschrift*, No. 16, 1888; reprinted from the *Medical Chronicle*, August.

water or chloroform water. All the animals died within 48 hours when water alone was used, and the others which had been treated with chloroform water and anthrax blood remained quite healthy. The reagent had no action on the *spores* of anthrax.

The action on comma bacilli is so energetic that a fresh cholera cultivation, mixed with an equal volume of chloroform water, is disinfected at the end of a minute. The proof of this is that one fails to get any growth in peptone solutions, gelatin, and so on. This property of chloroform is of great use in the laboratory to keep urea solutions, aqueous solutions of various ferments, pathological fluids, and in artificial digestive experiments, especially with trypsin. [It will be useful to add a few drops of chloroform in preparing artificially digestive foods for patients, provided the vessel be kept well closed. The objectionable bitter taste will not be developed, and if the taste of the chloroform be objected to, it can be removed by a few minutes' boiling.] Also, chloroform water can be used instead of glycerin to make solutions of various ferments, as pepsin, trypsin, etc. [The use in pharmacy will strike every practitioner. I have used it, instead of rectified spirit, for keeping solutions of alkaloids, and also in the preparation of infusions.] It is a useful and cheap preservative for anatomical preparations, though it gradually becomes colored with hæmoglobin. This might be prevented in various ways, either by laying the specimen in strong alcohol for a short time previously, or by combining it with Grawitz's fluid. [Also by previously washing out the blood in a stream of water.]

Other uses are :—(a). To prepare solutions for subcutaneous injection ; (b) to employ it internally in diseases of the digestive organs depending on the presence of micro-organisms ; amongst others, cholera. [Possibly the benefit that many patients derive from stomachic mixtures containing chloroform water as the vehicle is due to its destructive action on various micro-organisms.] Salkowski gave a dog (36·8 kilos.) 200 cc. (about 6½ ounces) of chloroform water with its food for four days without producing any effect, so that in the treatment of a disease like cholera large quantities of chloroform water might be given. The author recommends it as a mouth wash. [For surgical purposes it is not adapted, because of the ready volatility of the reagent, but it might be useful for irrigation in cases of puerperal pyrexia and deep abscesses, though its effect on staphylococci is not yet known.]

A. JASPER ANDERSON.

MINUTE OF THE COLLEGE MEETING.

A stated meeting of the members of the College was held June 25th, at 4 P. M. Chas. Bullock, presiding—Seventeen members were present. The minute of the last stated meeting was read, and adopted, on motion. The minutes of the Board of Trustees for April, May and June, and the minute of a special meeting of the Trustees held were read, and as usual approved.

The action upon the cases of members reported, by the Treasurer as in arrears in annual payments, which was deferred from the last meeting, being again brought forward—it was on motion resolved to drop from the roll two names.

On motion, being offered by Dr. C. B. Lowe, it was resolved that the College appropriate a sum not exceeding fifty dollars to defray the incidental expenses incurred by the College Committee on the revision of the Pharmacopœia.

An election of delegates to the session of the American Pharmaceutical Association to be held in Detroit in September next being ordered, Prof. J. P. Remington, Chas. A. Heinitsh, of Lancaster, Jos. L. Lemberger, of Lebanon, Gustavus Pile, and William McIntyre were declared duly elected.

A report upon the character of the recent meeting of the Pennsylvania Pharmaceutical Association held at Titusville in June being asked for—the following verbal statement was made. "The meeting was larger in numbers than anticipated—the interest was fully maintained in the number of papers presented, and in the discussions—an accession of between 40 and 50 members being made to the roll of the Association—the social features formed as usual an attractive part of the enjoyment."

No other business being presented an adjournment here prevailed.

WILLIAM B. THOMPSON,
Secretary.

PROCEEDINGS OF STATE PHARMACEUTICAL ASSOCIATIONS.

The Georgia Pharmaceutical Association held its thirteenth annual meeting in the House of Representatives, Atlanta, July 11, President, G. W. Case in the chair. An address by Mayor Cooper, the president's address, and the reports of various committees occupied the first day's sessions. One of the most important steps taken was the action in regard to the establishment of a School of Pharmacy in Atlanta.

During the second day, when a number of papers were read, the sessions were held in the Sweet Water Park Hotel, at Piedmont, Chautauqua, where also the next annual meeting will be held on the second Tuesday of July, 1889.

Mr. W. S. Parks of Atlanta was elected president; the secretary and treasurer were re-elected.

The Ohio Pharmaceutical Association met at its tenth annual meeting at Columbus, June 12 to 14, and was welcomed by Mayor Bruck. The address by President S. E. Allen, and the reports of officers and committees were presented and disposed of. A number of papers were read and discussed, and several questions of trade interest received attention. Dr. A. B. Lyons who was present as a representative of the Michigan State Association, spoke warmly in favor of a joint meeting of the two associations, for which purpose Put-in-Bay would be admirably adapted. M. D. Fulton, of Bucyrus, was elected president for the ensuing year, and L. C. Hopp and Charles Huston were re-elected secretary and treasurer respectively. The next meeting will take place at Mansfield, on the first Tuesday of June, 1889.

The West Virginia Pharmaceutical Association met at Clarksburg, June 20th, President McWhorter in the chair. An address of welcome by Mayor Lee, the president's annual address, the reports of officers and of committees, and the reading of several papers occupied the attention of the meeting. The president, secretary and treasurer were re-elected officers for the ensuing year.

The following printed Proceedings have been received :

Kansas.—Pp. 129. See July number, p. 376.

Louisiana.—Pp. 113. See July number, p. 376.

Nebraska.—Pp. 124. See July number, p. 377.

New York.—Pp. 232. See August number, p. 426.

Pennsylvania.—Pp. 170. See July number, p. 378.

EDITORIAL DEPARTMENT.

THE ORIGIN OF PETROLEUM.—In the interesting address by Mr. A. H. Samuel, published in our April number (pp. 187-197), there will be found a concise review of the various theories which have been advanced in explanation of the origin of petroleum. Against the formation of this natural product from organic material a weighty objection had been advanced pointing to the fact that, if petroleum really were a distillation-product of organic matter, the residues which should have remained of such matter had never been found. The weight of this argument has been considerably reduced by the results of experiments made by C. Engler in the laboratory at Karlsruhe, and reported in *Berichte der Deutschen Chemischen Gesellschaft*, 1888, pp. 1816-1827. We cannot follow the arguments of this interesting essay, and must content ourselves with a few brief references.

Referring to the views of various scientists who, for either chemical reasons, or for geological considerations, insist upon the formation of petroleum at a comparatively low temperature, but under a high pressure, the author had occasion to distil under such conditions a large quantity (492 kilos) of American fish oil, the pressure being gradually reduced from 10 to 4 atmospheres, while the temperature was increased from 320° to a little over 400° C. The products consisted of inflammable gases, of a watery liquid, and of an

oily portion amounting to about 60 per cent. This portion is described as brownish, in thin layers transparent, fluorescent with a green color, and of the specific gravity 0.8105; the odor is not unpleasant, and is free from the pungency of acrolein. It has as yet been only partially examined; but the hydrocarbons pentane, hexane, heptane, octane and nonane have been obtained from the lower boiling fractions.

Similar results, without carbonaceous residues, are obtained from olein and stearin if heated in sealed glass tubes of which the branches for condensation are bent downward, and are not immersed in the bath. These fats, and more particularly the fat acids, are of such composition, that if the oxygen be removed through combination with the requisite hydrogen for the formation of water, the remaining carbon and hydrogen will be in the proportion very nearly of 87:13, which is also the proportion of these elements in petroleum. Assuming that petroleum originates from the fat of fossil marine animals, the absence of acrolein and the lower fat acids may be explained by their removal with water, and carbonaceous residues cannot exist, because none were formed. Attention is also drawn to the durability of fatty substances in nature through the formation of adipocire. The presence of nitrogen compounds in some rock oils is also regarded as an indication of the origin from animal fat residues.

Explosive Mixture.—A serious accident happened in Topeka, Kansas, on the morning of August 14th, when Dr. Detlor, a veterinary surgeon, attempted to powder in an iron mortar a quantity of saltpetre and sulphur. On striking the mixture with an iron pestle a violent explosion took place, shattering the mortar and resulting, besides serious damage to property, in the wounding of the operator, whose left hand was completely blown off, the right hand pierced and mutilated, and a leg and other parts of the body lacerated. Several other persons were more or less seriously injured and a horse on the opposite side of the street was wounded.

An *International Congress of Hydrology and Climatology* is to be held in Paris, France, in 1889, the precise date to be announced hereafter. The director of the meteorological observatory of the Parc du Saint-Maur, Mr. E. Renou, is president of the committee, and Dr. F. de Ranse, Paris, is general secretary. Both national and foreign members are required to pay a contribution of 12 francs. The questions which have thus far been proposed for discussion are as follows:

a. Scientific Hydrology.

1. The precise determination of the temperature of thermal springs.
2. Micro-organisms in mineral waters, and their influence upon the composition and properties of the latter.
3. Influence of bacteriologic discoveries upon thermal therapeutics.
4. Program of the study of hydrology.

b. Medical Hydrology.

The questions refer mostly to the use of thermal and other mineral springs in the treatment of diseases of the heart and blood vessels, of kidney diseases, neuralgias, some forms of tuberculosis, etc.

c. Climatology.

The proposed questions embrace the conditions for the organization of meteorological observatories; climatology of sanitary stations, their comparison and classification; influence of the climate of high localities upon pulmonary affections, and of maritime climates upon tuberculosis.

The Chicago College of Pharmacy held its summer commencement in the Grand Opera House, July 31st; one lady and thirty-two gentlemen graduated. Addresses were made by Hon. B. R. Smith, T. W. Sanders, W. K. Forsythe, and Professors Bastin and Garrison.

The University of Michigan had its annual commencement June 28th, when twenty-three persons, including one lady, graduated from the School of Pharmacy as Pharmaceutical Chemists.

Hair Tonic.—Quinine sulphate 60 grains; oil of cajeput 2 drachms; attar of rose 10 drops; bay rum 1 pint; lanolin $\frac{1}{2}$ ounce. To be applied to the scalp with vigorous brushing twice a week.

Numerous formulas of a similar character are in use. The above was prescribed under the supposition that a perfect solution would be formed, which is impossible owing to the insolubility of lanolin in the bay rum. Similar hair tonics are sometimes made with a stronger alcoholic menstruum and sufficient castor oil to form a clear solution at ordinary temperatures; and chinoidine or alcoholic extract of cinchona is used in place of quinine.

REVIEWS AND BIBLIOGRAPHICAL NOTICES.

Annual of the Universal Medical Sciences.—A yearly report of the progress of the general sanitary sciences throughout the world. Edited by Charles E. Sajous, M. D., lecturer on Laryngology and Rhinology in Jefferson Medical College, Philadelphia; and seventy associate editors, assisted by over two hundred corresponding editors, collaborators and correspondents. Philadelphia and London. F. A. Davis, publisher, 1888.

The first issue of this annual makes its appearance in five handsome octavo volumes, of about 550 pages each. Its early publication was made possible only through official collaboration by a large number of competent men. The subject matter reported upon is necessarily classified according to diseases, or rather classes of diseases, and each head is intended to contain all the observations made on the subject during the preceding year. That this intention has been carried out, may be inferred from the names of the editors, printed upon seven pages of the preliminary portion in the first volume. The work is printed with clear types upon heavy paper and is illustrated with numerous wood cuts, chromolithographs, maps, etc.

Aside from the completeness and reliability of the work due to the care of the collaborators, it has several peculiar features, which facilitate its use. Thus, the table of contents of each volume is found upon the back of the cover; and the index to the whole work has been made in three columns, the first of which gives the general references while in the second are found therapeutical observations and suggestions, and in the third column the names of authors quoted in connection with the general subjects.

This annual will doubtless become an important repository of the researches, observations and progress in the various departments of the medical sciences.